The specification was amended to reflect the current address of ATCC and to correct a minor typographical error.

Claims

Support for the amendments to claims 39 and 44 may be found in the specification, for example, at section F, parts 2 and 4. For example, the specification at Section F, in the first paragraph of part 2, discloses that lymphocytes may be used for "producing antibodies that will specifically bind to the immunizing agent." The specification at Part F, first sentence of section 4 states: "Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens."). No new matter is added by way of the amendments.

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 39 and 44 were rejected as indefinite in that claim 39 recites "binding" and claim 44 recites "specific binding" to the polypeptide of Figure 118, the Examiner stating that antibody binding is a "specific" event. Claims 39 and 44 have been amended so that both claims now recite an antibody that specifically binds to the polypeptide of Figure 118; amended claim 44 further recites that the antibody is a bispecific antibody that binds to a second antigen. Accordingly, Applicants respectfully submit that the rejections to claims 39 and 44 as indefinite are overcome.

Claim Rejections - 35 USC § 101

Claims 39-44 were rejected under 35 USC § 101, since "the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility." The rejection of claims 39-44 is respectfully traversed.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II

(B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for antibodies that bind to the PRO339 polypeptide.

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 8 (pages 230-234 of the specification), including primary lung cancers and colon cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification. PRO339 showed 2-3 fold gene amplification in a number of lung and colon tumors.

In assessing the value of these data, the Examiner notes that: "There is no specific information on what type of the normal tissue was used as a control and how many normals there were. A single normal sample is not sufficient for basing relative levels of many other samples." The Examiner has apparently overlooked that, as discussed above, control DNA was pooled from the cells of ten normal healthy individuals (page 222, lines

34-36). Accordingly, the results are not based on a single normal sample. The samples were obtained from blood cells as it is usual in similar gene amplification assays.

The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ real-time PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The facts disclosed in the Declaration also confirm that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO339 is a diagnostic marker of human lung and colon cancer. It is, of course, true that further research would be needed to develop PRO339 and antibodies that bind to it into a diagnostic product. Such follow-up tests could include the mapping of the PRO339 gene to a chromosome, which could be followed, for example, by dual-color FISH with DNA probes complementary to the PRO339 gene and the centromere of the chromosome to distinguish a locus-specific gene amplification from chromosome aneuploidity. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that antibodies that bind PRO339 lack patentable utility.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility is viewed to be "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO339 is a diagnostic marker of lung and colon cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based are not inconsistent with the logic underlying the assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fail, and never make it into a drug product. However, the USPTO is not the

FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Thus, Applicants respectfully submit that antibodies that bind PRO339 may be used in diagnostic markers for identifying lung cancer or colon cancer, and thus that the specification discloses at least one credible substantial and specific utility for antibodies that bind to PRO339 Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections under 35 U.S.C. 112, first paragraph

(a) Claims 39-44 were rejected under 35 USC § 112, first paragraph "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that the specification discloses a substantial, specific and credible utility for antibodies that bind to the PRO339 polypeptide. Applicants respectfully submit that it would not require undue experimentation for one of skill in the art to apply the teachings of the present disclosure so as to practice the invention by using antibodies that bind to the polypeptide shown in Figure 118 (SEQ ID NO.:339. The Examiner has named no particular reasons why the specification would not be enabling for the use now recited in the claims. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims on this ground.

35 USC §§ 102 and 103

The rejection of Claims 39 and 44 under 35 U.S.C. § 102 (b)

Claims 39-44 were rejected under 35 USC 102(b) as "being anticipated by WO 99/63088" which is said by the Examiner to disclose antibodies "that would be reasonably expected to bind the polypeptide with the sequence of SEQ ID NO:339 of the instant application because the proteins share large regions of high identity."

Anticipation under 35 U.S.C. § 102 requires that "every element of the claimed invention be identically shown in a single reference." (*In re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990). However, WO 99/63088 nowhere discloses a polypeptide of SEQ ID NO:339, and nowhere discloses antibodies that specifically bind to the polypeptide shown in Figure 118 (SEQ ID NO:339). As is known to those of ordinary skill in the art, an antibody that specifically binds to its target antigen does so without substantial cross-reactivity with another antigen. For example, referring to antibodies raised against an epitope tagged polypeptide, the present specification states "the antibody does not substantially cross-react with other epitopes" (page 74, lines 34-35). Thus, an antibody that binds both to the polypeptide of Figure 118 (SEQ ID NO:339) and to the cited polypeptide of WO 99/63088 would not be one that specifically bound to either polypeptide and these would not be within the scope of the present claims. Thus, Applicants respectfully submit that the antibodies claimed in the present application, which specifically bind to the polypeptide shown in Figure 118 (SEQ ID NO:339), are not anticipated by WO 99/63088.

Accordingly, lacking at least these elements of claims 39-44, Applicants respectfully submit that the rejection of claims 39-44 under 35 U.S.C. § 102 (b) is overcome.

The Rejection of Claims "50 and 51" under 35 USC § 103(a)

Claims "50 and 51" were rejected under 35 USC § 103(a) "as being unpatentable over GenBank Accession No. BAA92640 in view of Sibson et al. (WO 94/01548) and Godowski et al. (US Patent 6,030,831)." However, as the instant application contains neither a claim 50 nor a claim 51, it is unclear which pending claims, if any, this rejection is directed towards.

Applicants acknowledge the Examiner's statement that GenBank Accession No. BAA92640 does not teach an antibody that binds a peptide. GenBank Accession No. BAA92640 is discussed below with respect to the rejection of claims 39-44 under 35 USC § 103(a).

The Rejection of Claims 39-44 under 35 USC § 103(a)

Claims 39-44 were rejected under 35 USC § 103(a) "as being unpatentable over GenBank Accession No. BAA92640 in view of "Applicants' Admission on p.34, lines 5-6 and Fleming et al. (Dev., 124:2873-81,1997) and Godowski et al. (US Patent 6,030,831)."

According to the Office Action, the effective date of the primary reference (GenBank Accession No. BAA92640) is March 14, 2000. The gene amplification data, which support the utility of the polypeptides claimed in the present application were first disclosed in PCT/US00/03565 filed on February 11, 2000, the priority of which is claimed in the present application. Since the present application is entitled to at least the February 11, 2000 priority, GenBank Accession No. BAA92640 is not prior art. Accordingly, the present rejections should be withdrawn.

Applicant note the citation of additional art, which was not relied upon in any of the rejections. Since the present application is entitled to the February 11, 2000 priority,

WO2001153312 is not prior art. Similarly, none of the other references are believed to anticipate or render obvious any of the claims pending.

Attached hereto is a marked-up copy of the amendments made in the specification and claims. The attached sheets are entitled "**Version with Markings to Show Changes Made**."

All claims are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 08-1641.

Respectfully submitted,

Date: February 19, 2003

Ginger R. Dreger (Reg. No. 33,055)

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Version with Markings to Show Changes Made

In the Specification:

Replace the paragraph beginning at page 202, line 36 with the following amended paragraph:

A variety of protocols for measuring soluble or membrane-bound [PRo317] PRO317, using either polyclonal or monoclonal antibodies specific for that PRO317, are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), radioreceptor assay (RRA), and fluorescent activated cell sorting (FACS). A two-site monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on PRO317 is preferred, but a competitive binding assay may be employed. These assays are described, among other places, in Maddox *et al.* J Exp. Med., 158:1211 (1983).

Replace the paragraph beginning at page 250, line 1 with the following amended paragraph:

-- The following materials have been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD], 10801 University Boulevard, Manassas, VA 20110-2209, USA (ATCC):--

In the Claims:

Claims 39 and 44 have been amended as follows:

39. (Once amended) An antibody that specifically binds to the polypeptide shown in Figure 118 (SEQ ID NO:339).

44. (Once amended) The antibody of claim 39 which specifically binds to the polypeptide shown in Figure 118 (SEQ ID NO: 339), wherein said antibody is a bispecific antibody that also binds to another antigen.